

Fig. 1

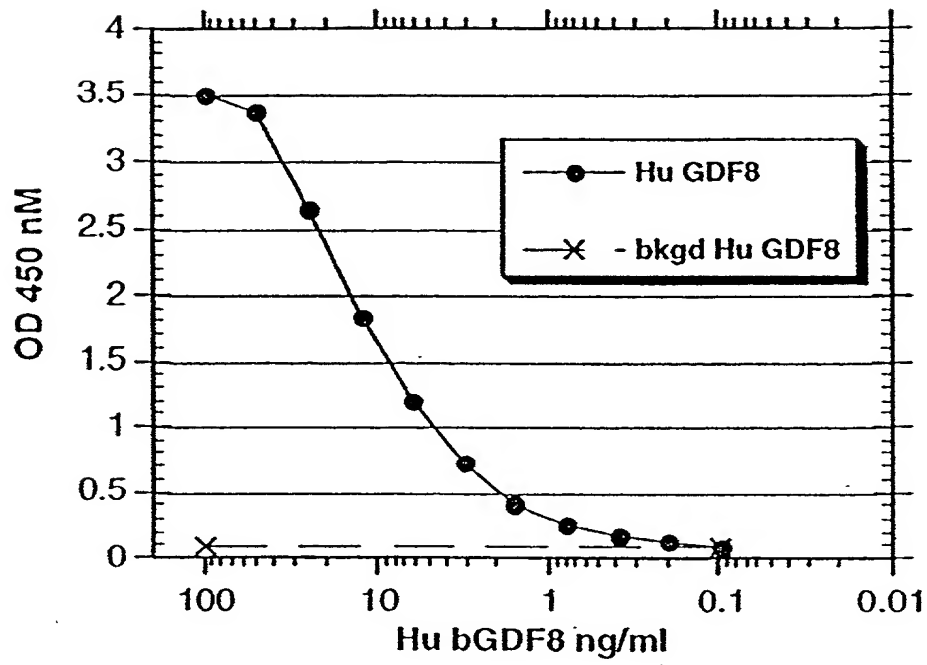


Fig. 2

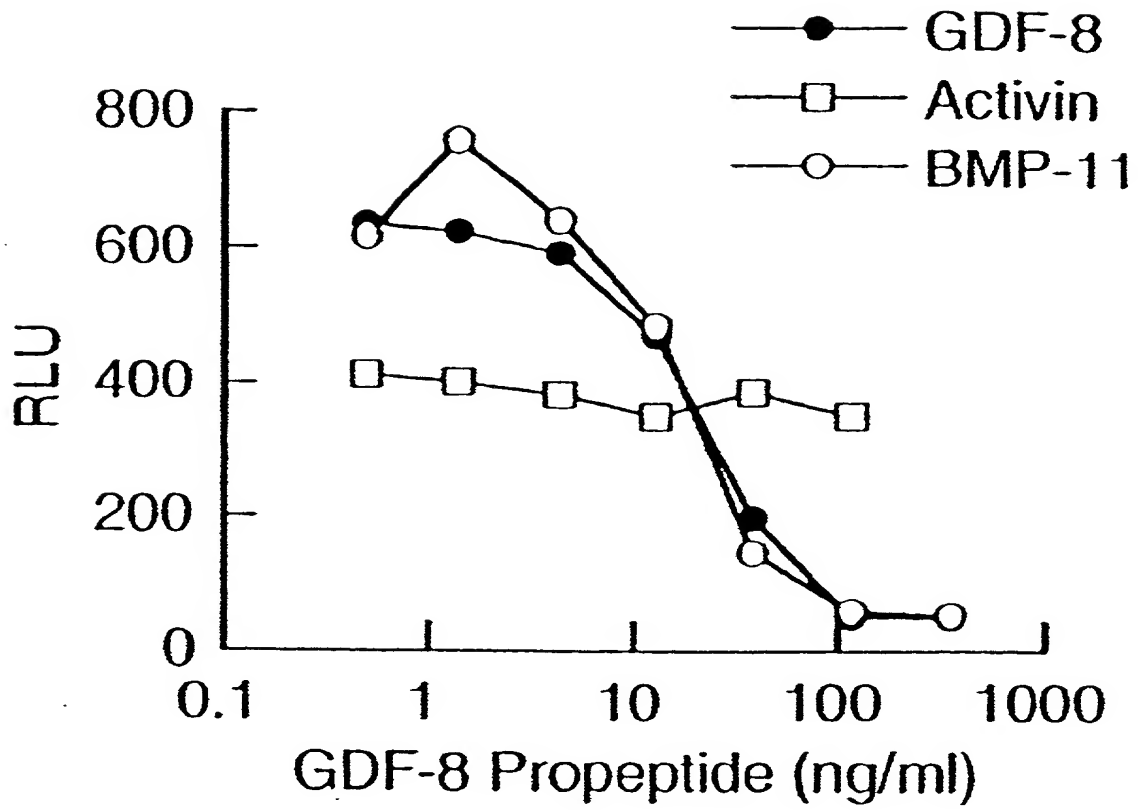


Fig. 3

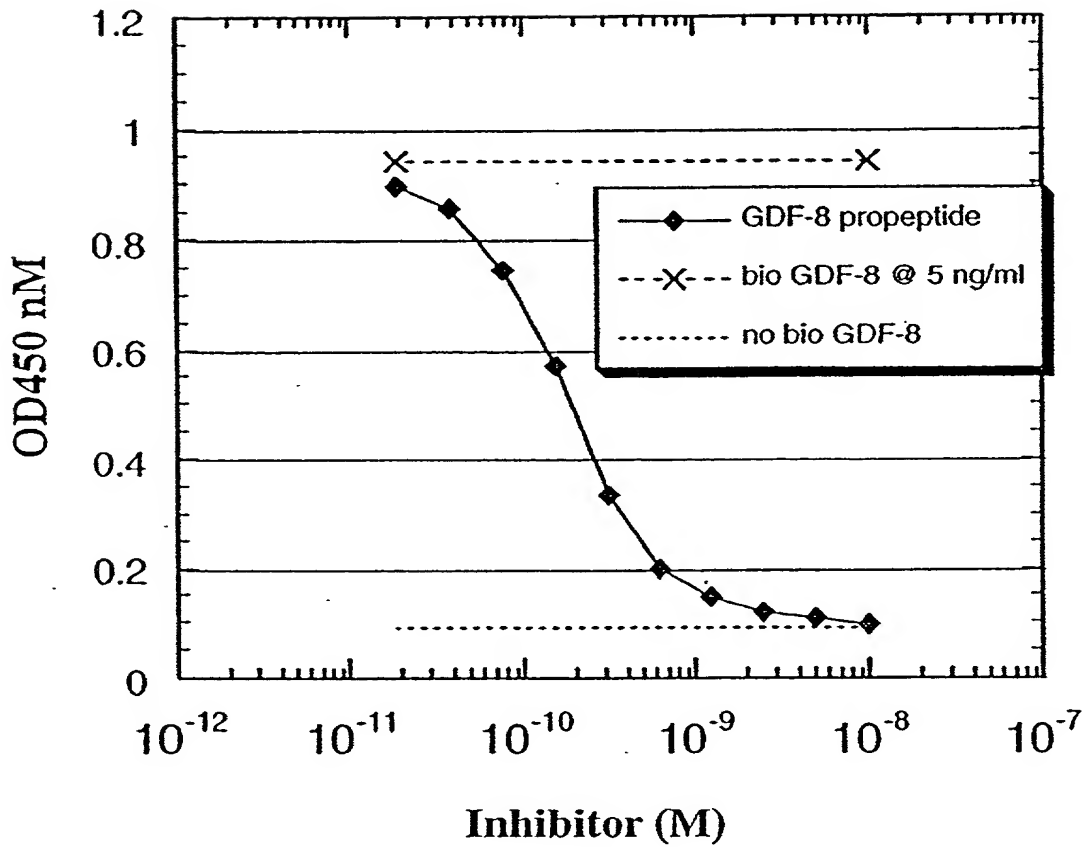


Fig. 4

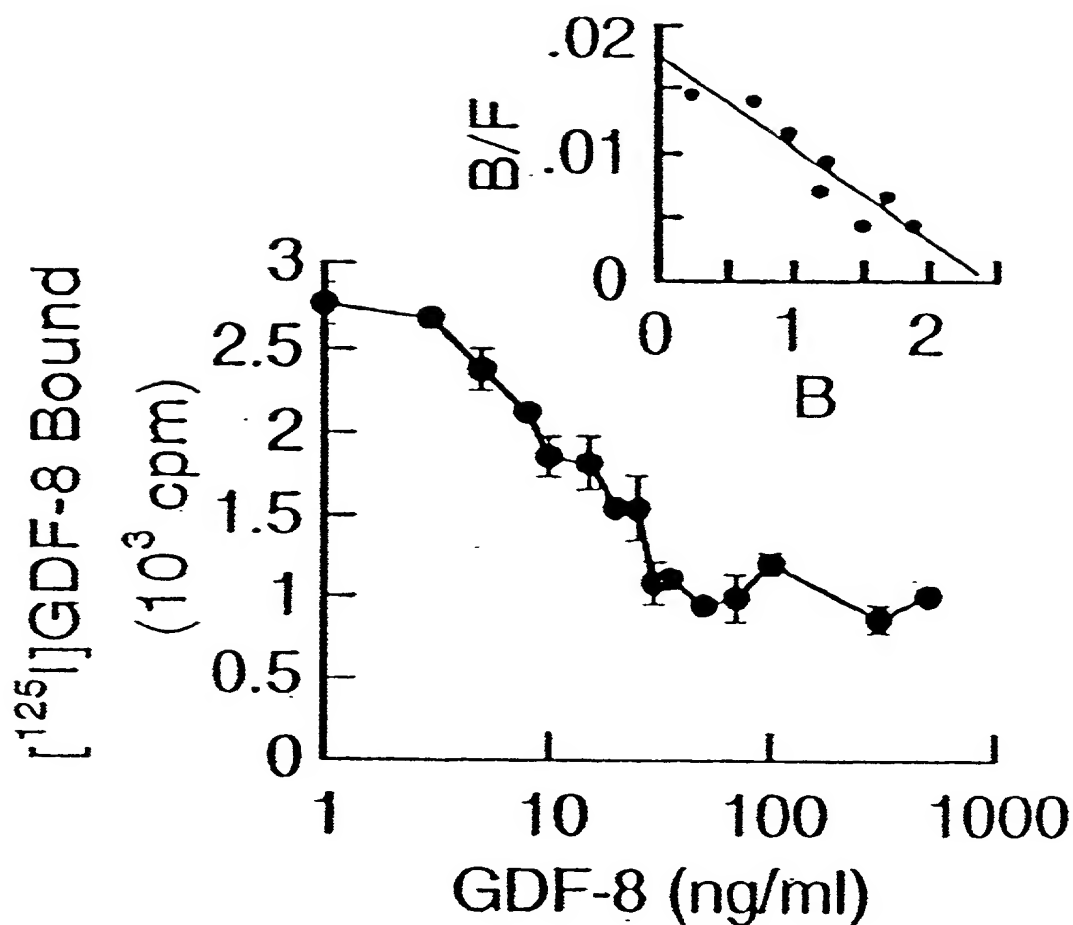


Fig. 5

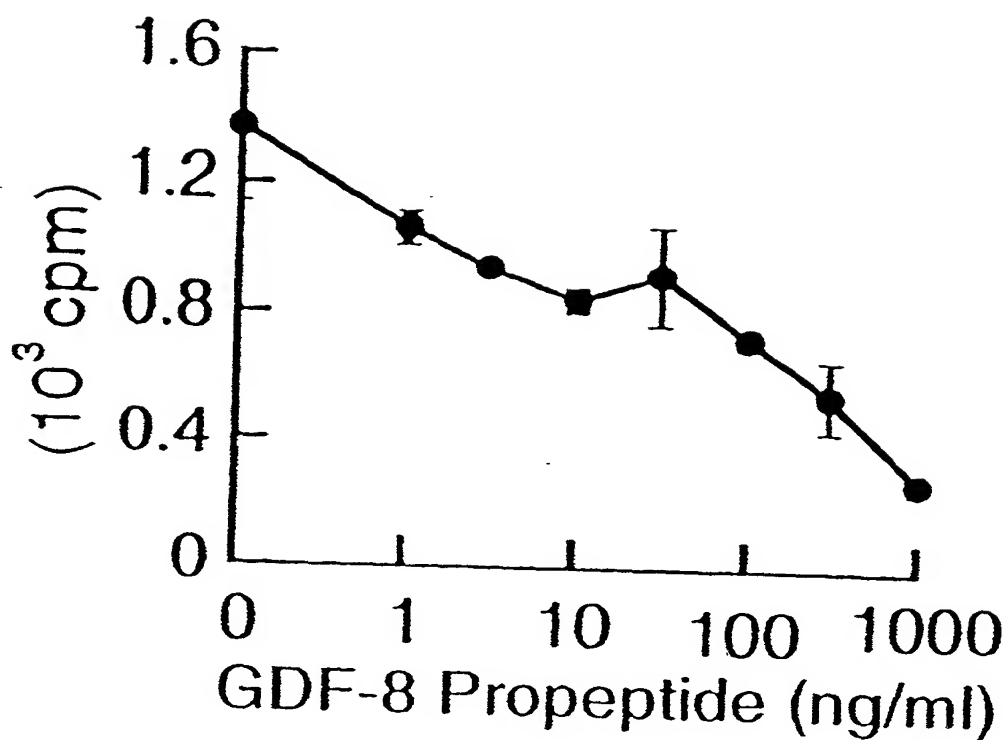


Fig. 6

NEGS	PKRS	EPRG	PGK
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Secretory Mu GDF-8 propeptide Mu IgG2a Fc
leader

MMQKLQMYVYIYLFMLIAAGPVDLNEGSEEREENVEKEGLCNACAWRQNTSYSRIEAIKILSKLRLET
APNISKDAIRQLLPRAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIITMPTESDFLMQADGKPKC
CFFKFSKIQYNKVVKAQLWIYLRPVKTPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMSGTGIWQSI
DVKTVLQNLWKQPESNLIGIEIKALDENGHDLA VTFPGGEDGLNPFLEVKTDTPKRSEPRGPTIKPCP
PCKCPAPNLEGGPSVFIFPPKIKDVLMSLSPIVTCVVDVSEDDPDVQISWFFVNNVEVHTAQITQTHRE
DYNSTLRVVSALPIQHODWMSGKAFACAVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMTKKQV
TLTCMVTDFMPEDIYVEWTNNGKTELNYKNTPEVLDSGYSFYMSKLRVEKKNWVERNSYSCSVVHEGL
HNHHTTKSFSRTPGK

Fig. 7A

NEGS	PKRS	GS GS	EPRG	PGK
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Secretory Mu GDF-8 propeptide Mu IgG2a Fc
leader

MMQKLQMYVYIYLFMLIAAGPVDLNEGSEEREENVEKEGLCNACAWRQNTSYSRIEAIKILSKLRLET
APNISKDAIRQLLPRAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIITMPTESDFLMQADGKPKC
CFFKFSKIQYNKVVKAQLWIYLRPVKTPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMSGTGIWQSI
DVKTVLQNLWKQPESNLIGIEIKALDENGHDLA VTFPGGEDGLNPFLEVKTDTPKRSGSGSEPRGPTI
KPCPPCKPAPNLEGGPSVFIFPPKIKDVLMSLSPIVTCVVDVSEDDPDVQISWFFVNNVEVHTAQITQ
THREDYNSTLRVVSALPIQHODWMSGKAFACAVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEMT
KKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKNTPEVLDSGYSFYMSKLRVEKKNWVERNSYSCSVV
HEGLHNHHTTKSFSRTPGK

Fig. 7B

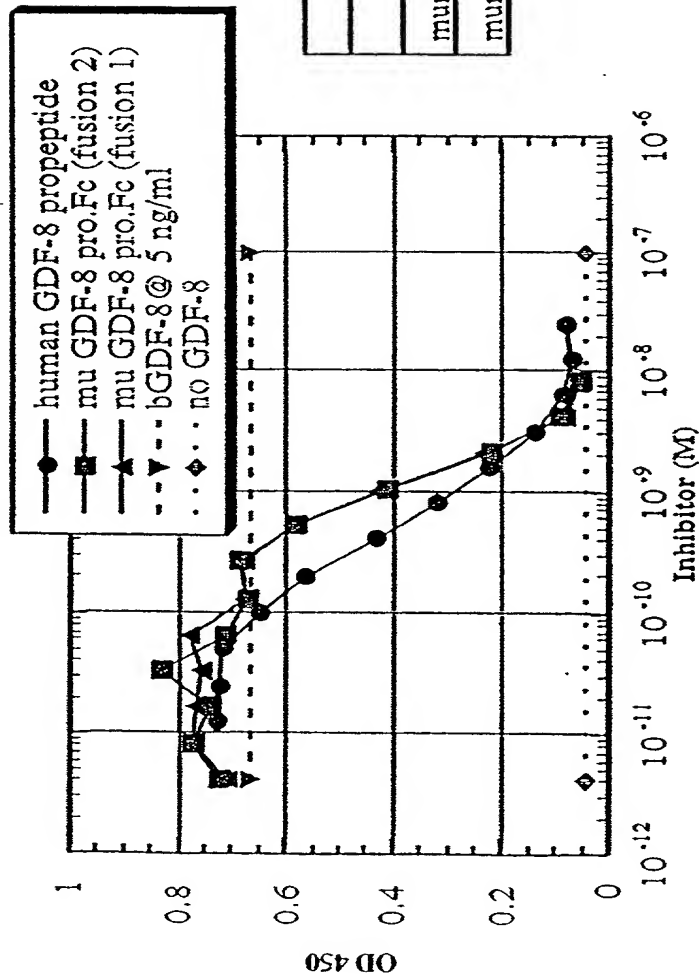


Fig. 8 A

Fig. 8 B

Inhibitor	IC50 (M)
hu GDF-8 propeptide	6×10^{-10}
murine GDF-8 pro.Fc (Fusion 1)	1.3×10^{-9}
murine GDF-8 pro.Fc (Fusion 2)	1.3×10^{-9}

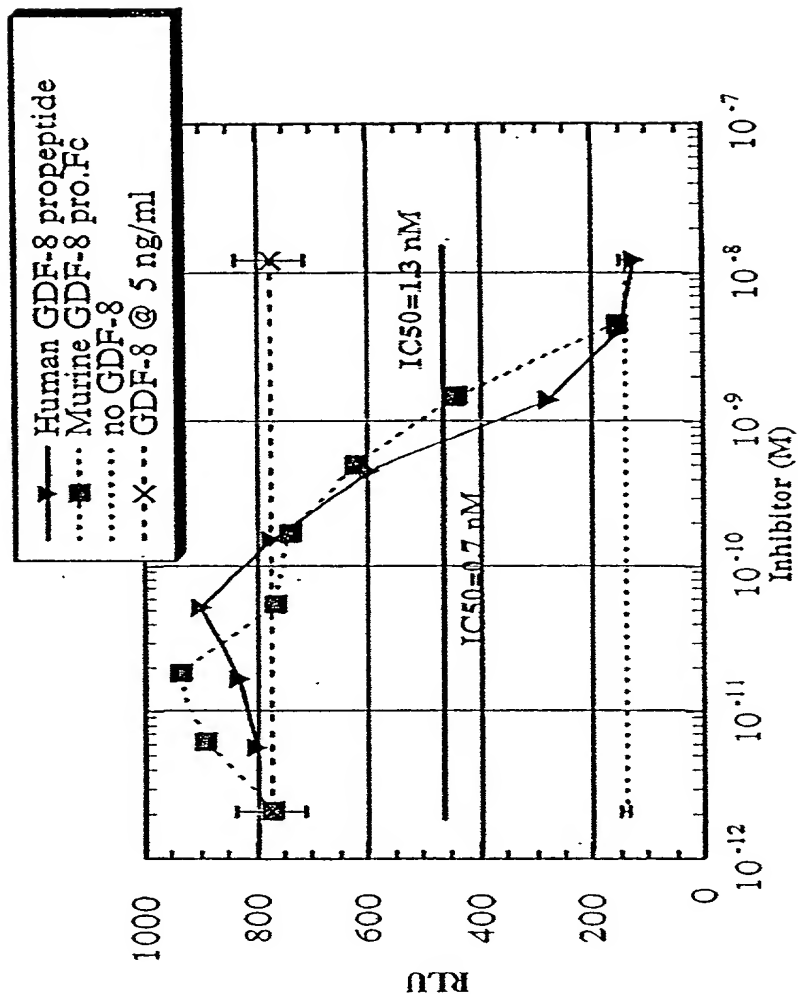


Fig. 9

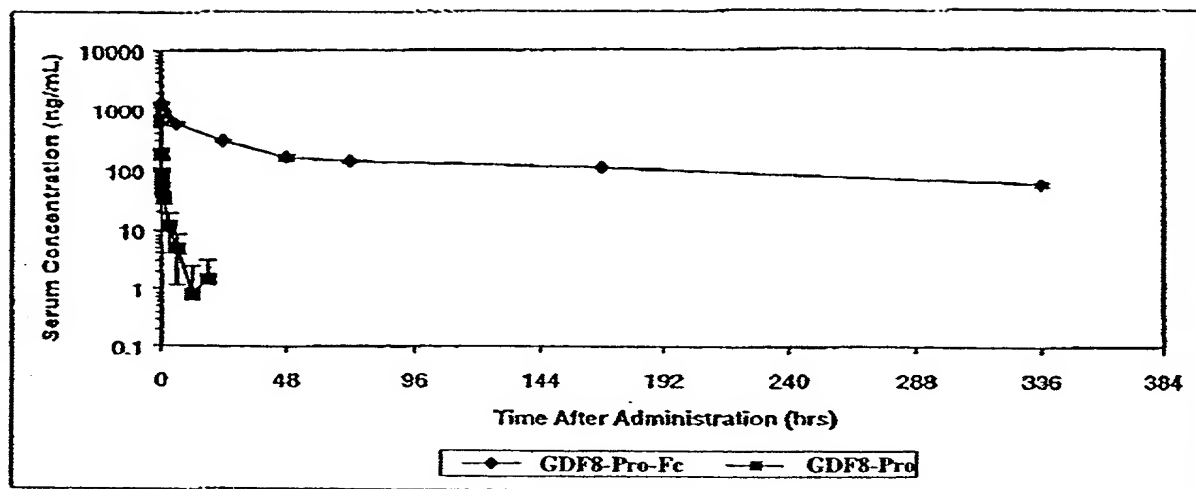


Fig. 10

	NENS	PKRS	EPKS	PGK
Secretory	Hu GDF-8 propeptide			Hu IgG1 Fc
leader				

MQKLQLCVYIYLFMLIVAGPVLDLNENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQLSKLRLETAPN
 ISKDVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIIITMPTESDFLMQVDGKPKCCFFKF
 SSKIQYNKVVKQAQLWIYLRPVETPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMPGTGIWQSIDVKTVLQ
 NWLKPESNLGIEIKALDENGHDLA VTFPGGEDGLNPFLEVKVTDTPKRSEPKSCDKTHTCPPCPAPELL
 GGPSVFLFPPKPKDTLMISRTPETCVVDVSHEDPEVKFNWYVDGVEVHNATKTPREEQYNSTYRVVSVL
 TVLHQDWLNGKEYCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDI
 AVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSVMTHEALHNHYTQKSLSLSPGK

Fig. 11A

	NENS	PKRS	DKT	PGK
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Secretory leader Hu GDF-8 propeptide

Hu IgG1 Fc mutated

MQKLQLCVYIYLFMLIVAGPVVDLNNSENSEKQENVEKEGLCNACTWRQNTKSSRIEAIKIQILSKLRLETAPN
 ISKDVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIIITMPTESDFLMQVDGKPKCCFFKF
 SSKIQYNKVVKVKAQLWIYLRPVETPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMPGTGIWQSIDVKTVLQ
 NWLKQPESNLGIKALDENNGHDLAVTFPPGPGEDGLNPFLEVKVTDTPKRSDKTHTCPPCPAPEALGAPSV
 FLFPKPKD¹TLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQ
 DWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWE
 SNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNV²VFSCVMHEALHNHYTQKSLSLSPGK

Fig. 11B

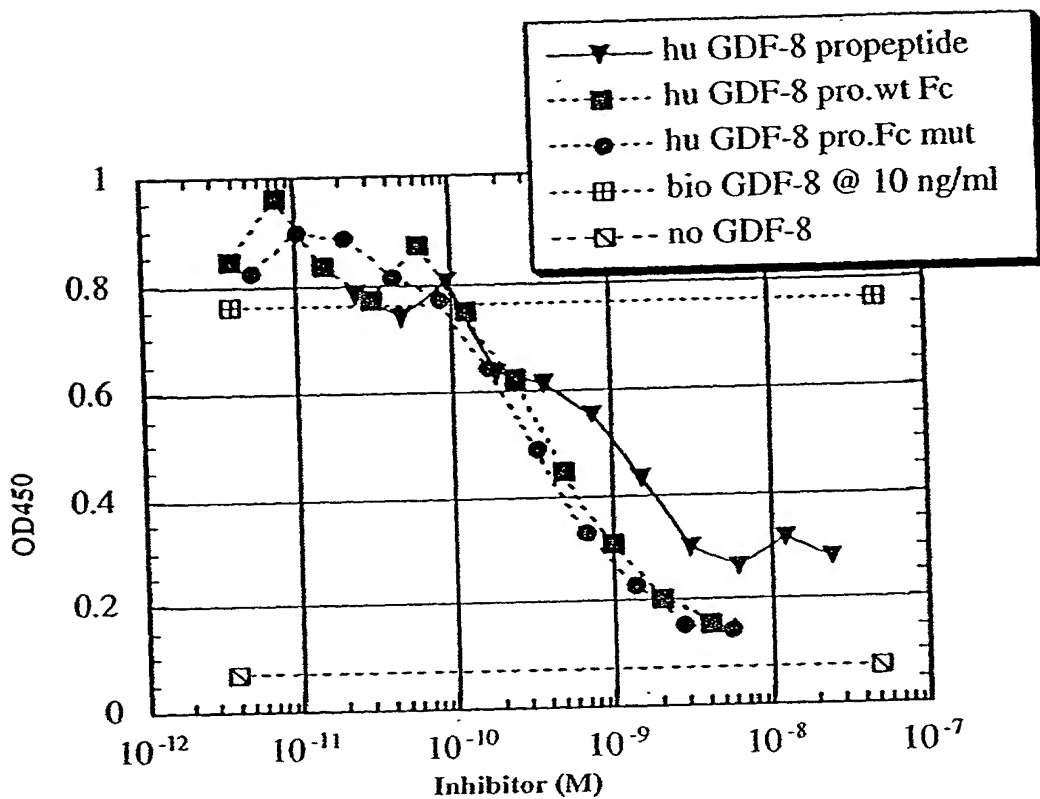


Fig. 12

Dissected Tissue Mass

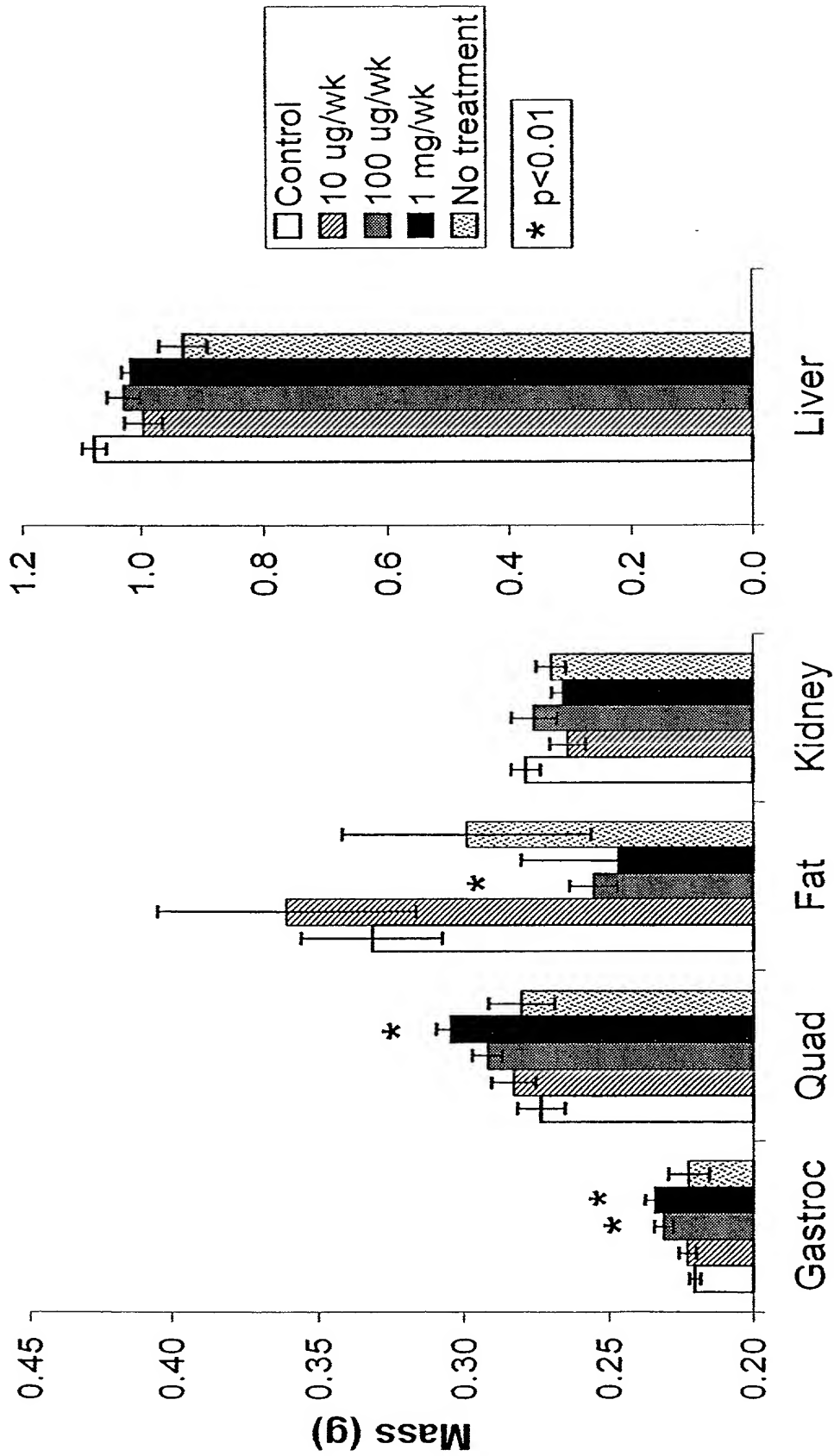


Figure 13

Fig. 14A

SEQ ID NO:1 Human GDF-8 precursor protein - protein
sequence

MQKLQLCVYIYLFMLIVAGPVDLNENSEQKENVEKEGLCNACTWRQNTKSS
RIEAIKIQILSKLRLETAPNISKDVIRQLLPKAPPLRELIDQYDVQRDDSS
DGSLEDDDYHATTETIITMPTESDFLMQVDGKPKCCFFKFSSKIQYNKVVK
AQLWIYLRPVETPTTVFVQILRLIKPMKDGTRYTGIRSLKLDMNPGTGIWQ
SIDVKTVLQNLWKQPESNLGIEIKALDENGHD LAVTFPGPGEDGLNPFLEV
KVTDTPKRSRRDFGLDCDEHSTESRCCRYPLTVDFEAFGWDWIIAPKRYKA
NYCSGECEFEVFLQKYPHTHLVHQANPRGSAGPCCTPTKMSPINMLYFNGKE
QIIYGKIPAMVVDRCGCS

Fig. 14B

SEQ ID NO:2 Human GDF-8 precursor protein - DNA
sequence

ATGCAAAAACCTGCAACTCTGTGTTTATATTTACCTGTTTATGCTGATTGT
TGCTGGTCCAGTGGATCTAAATGAGAACAGTGAGCAAAAAGAAAATGTGG
AAAAAGAGGGGCTGTGTAATGCATGTACTTGGAGACAAAACACTAAATCT
TCAAGAATAGAAGCCATTAAGATACAAATCCTCAGTAAACTTCGTCTGGA
AACAGCTCCTAACATCAGCAAAGATGTTATAAGACAACTTTTACCCAAAG
CTCCTCCACTCCGGGAACTGATTGATCAGTATGATGTCCAGAGGGATGAC
AGCAGCGATGGCTCTTTGGAAGATGACGATTATCACGCTACAACGGAAAC
AATCATTACCATGCCTACAGAGTCTGATTTTCTAATGCAAGTGGATGGAA
AACCCAAATGTTGCTTCTTTAAATTTAGCTCTAAAATACAATACAATAAA
GTAGTAAAGGCCCAACTATGGATATATTTGAGACCCGTCGAGACTCCTAC
AACAGTGTTTTGTGCAAATCCTGAGACTCATCAAACCTATGAAAGACGGTA
CAAGGTATACTGGAATCCGATCTCTGAAACTTGACATGAACCCAGGCACT
GGTATTTGGCAGAGCATTGATGTGAAGACAGTGTTGCAAAATTGGCTCAA
ACAACCTGAATCCAACCTTAGGCATTGAAATAAAAGCTTTAGATGAGAATG
GTCATGATCTTGCTGTAACCTTCCCAGGACCAGGAGAAGATGGGCTGAAT
CCGTTTTTTAGAGGTCAAGGTAACAGACACACCAAAAAGATCCAGAAGGGA
TTTTTGGTCTTGACTGTGATGAGCACTCAACAGAATCACGATGCTGTCGTT
ACCCTCTAACTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATCGCT
CCTAAAAGATATAAGGCCAATTACTGCTCTGGAGAGTGTGAATTTGTATT
TTTACAAAAATATCCTCATACTCATCTGGTACACCAAGCAAACCCAGAG
GTTTCAGCAGGCCCTTGCTGTACTCCCACAAAGATGTCTCCAATTAATATG
CTATATTTTAATGGCAAAGAACAAATAATATATGGGAAAATTCCAGCGAT
GGTAGTAGACCGCTGTGGGTGCTCA

Fig. 14C

SEQ ID NO:3 Human mature GDF-8 - protein sequence

DFGLDCDEHSTESRCCRYPLTVDFEAFGWDWIIAPKRYKANYCSGECEVFV
LQKYPHTHLVHQANPRGSAGPCCTPTKMSPINMLYFNGKEQIIYGKIPAMV
VDRCGCS

Fig. 14D

SEQ ID NO:4 Human mature GDF-8 - DNA sequence

GATTTTGGTCTTGACTGTGATGAGCACTCAACAGAATCACGATGCTGTCTG
TTACCCTCTAACTGTGGATTTTGAAGCTTTTGGATGGGATTGGATTATCG
CTCCTAAAAGATATAAGGCCAATTACTGCTCTGGAGAGTGTGAATTTGTA
TTTTTACAAAAATATCCTCATACTCATCTGGTACACCAAGCAAACCCAG
AGGTTTCAGCAGGCCCTTGCTGTACTCCACAAAGATGTCTCCAATTAATA
TGCTATATTTTAATGGCAAAGAAATAATATATGGGAAAATTCCAGCG
ATGGTAGTAGACCGCTGTGGGTGCTCA

Fig.14E

SEQ ID NO:5 Human GDF-8 propeptide - protein
sequence

NENSEQKENVEKEGLCNACTWRQNTKSSRIEAIKIQILSKLRLETAPNISK
DVIRQLLPKAPPLRELIDQYDVQRDDSSDGSLEDDDYHATTETIITMPTES
DFLMQVDGKPKCCFFKFSSKIQYNKVVKQALWIYLRPVETPTTVFVQILRL
IKPMKDGYTRYTGIRSLKLDMNPGTGIWQSIDVKTVLQNLKQPESNLGIEI
KALDENGHDLAVTFPGPGEDGLNPFLEVKVTDTPKRSRR

Fig. 14F

SEQ ID NO:6 Human GDF-8 propeptide - DNA sequence

AATGAGAACAGTGAGCAAAAAGAAAATGTGGAAAAAGAGGGGCTGTGTAAT
GCATGTACTTGGAGACAAAACACTAAATCTTCAAGAATAGAAGCCATTAAG
ATACAAATCCTCAGTAACTTCGTCTGGAAACAGCTCCTAACATCAGCAAA
GATGTTATAAGACAACCTTTTACCCAAAGCTCCTCCACTCCGGGAACTGATT
GATCAGTATGATGTCCAGAGGGATGACAGCAGCGATGGCTCTTTGGAAGAT
GACGATTATCACGCTACAACGGAAACAATCATTACCATGCCTACAGAGTCT
GATTTTCTAATGCAAGTGGATGGAAAACCCAAATGTTGCTTCTTTAAATTT
AGCTCTAAAATACAATAACAATAAAGTAGTAAAGGCCCAACTATGGATATAT
TTGAGACCCGTCGAGACTCCTACAACAGTGTTTGTGCAAATCCTGAGACTC
ATCAAACCTATGAAAGACGGTACAAGGTATACTGGAATCCGATCTCTGAAA
CTTGACATGAACCCAGGCACTGGTATTTGGCAGAGCATTGATGTGAAGACA
GTGTTGCAAAATTGGCTCAAACAACCTGAATCCAACCTTAGGCATTGAAATA
AAAGCTTTAGATGAGAATGGTCATGATCTTGCTGTAACCTTCCCAGGACCA
GGAGAAGATGGGCTGAATCCGTTTTTTAGAGGTCAAGGTAACAGACACACCA
AAAAGATCCAGAAGG

Fig. 14G

SEQ ID NO:7 Human BMP-11 precursor protein -
protein sequence

MVLAAPLLLGFLLLALRLRPRGEAAEGPAAAAAAAAAAAAAAAAAGVGGERSSRP
APSVAPEPDGCPVCVWRQHSRELRLSEIKSQILSKLRLKEAPNISREVVKQ
LLPKAPPLQQILDLHDFQGDALQPEDFLEEDEYHATTETVISMASETDPVAV
QTDGSPLCCHFHFSPKVMFTKVLKAQLWVYLRPVPRPATVYLLQILRLKPLT
GEGTAGGGGGRRHIRIRSLKIELHSRSGHWQSIDFKQVLHSWFRQPQSNW
GIEINAFDPSGTDLAVTSLGPGAEGLPFMELRVLENTKRSRRNLGLDCDE
HSSESRCRYPLTVDFEAFGWDWIIAPKRYKANYCSGQCEYMFQKYPHTH
LVQQANPRGSAGPCCTPTKMSPINMLYFNDKQQIIYGKIPGMVVDRCGCS

Fig. 14H

SEQ ID NO:8 Human BMP-11 precursor protein - DNA
sequence

ATGGTGCTCGCGGGCCCCGCTGCTGCTGGGCTTCCTGCTCCTCGCCCTGGA
GCTGCGGGCCCCGGGGGGAGGCGGCCGAGGGCCCCGCGGCGGCGGCGGCGG
CGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGGCGG
CCAGCCCCGTCCGTGGCGCCCCGAGCCGGACGGCTGCCCCGTGTGCGTTTG
GCGGCAGCACAGCCGCGAGCTGCGCCTAGAGAGCATCAAGTCGCAGATCT
TGAGCAAACCTGCGGCTCAAGGAGGCGCCCAACATCAGCCGCGAGGTGGTG
AAGCAGCTGCTGCCCAAGGCGCCGCGCTGCAGCAGATCCTGGACCTACA
CGACTTCCAGGGCGACGCGCTGCAGCCCGAGGACTTCCTGGAGGAGGACG
AGTACCACGCCACCACCGAGACCGTCATTAGCATGGCCCAGGAGACGGAC
CCAGCAGTACAGACAGATGGCAGCCCTCTCTGCTGCCATTTTCACTTCAG
CCCCAAGGTGATGTTACAAAGGTACTGAAGGCCAGCTGTGGGTGTACC
TACGGCCTGTACCCCGCCAGCCACAGTCTACCTGCAGATCTTGCGACTA
AAACCCCTAACTGGGGAAGGGACCGCAGGGGGAGGGGGCGGAGGCCGGCG
TCACATCCGTATCCGCTCACTGAAGATTGAGCTGCACTCACGCTCAGGCC
ATTGGCAGAGCATCGACTTCAAGCAAGTGCTACACAGCTGGTTCCGCCAG
CCACAGAGCAACTGGGGCATCGAGATCAACGCCTTTGATCCCAGTGGCAC
AGACCTGGCTGTACCTCCCTGGGGCCGGGAGCCGAGGGGCTGCATCCAT
TCATGGAGCTTTCGAGTCCTAGAGAACACAAAACGTTCCCGGCGGAACCTG
GGTCTGGACTGCGACGAGCACTCAAGCGAGTCCCGCTGCTGCCGATATCC
CCTCACAGTGGACTTTTGAGGCTTTTCGGCTGGGACTGGATCATCGCACCTA
AGCGCTACAAGGCCAACTACTGCTCCGGCCAGTGCGAGTACATGTTTCATG
CAAAAATATCCGCATACCCATTTGGTGCAGCAGGCCAATCCAAGAGGCTC
TGCTGGGGCCCTGTTGTACCCCCACCAAGATGTCCCAATCAACATGCTCT
ACTTCAATGACAAGCAGCAGATTATCTACGGCAAGATCCCTGGCATGGTG
GTGGATCGCTGTGGCTGCTCT

Fig. 14I

SEQ ID NO:9 Human BMP-11 mature - protein sequence

NLGLDCDEHSSESRCRYPLTVDFEAFGWDWI IAPKRYKANYCSGQCEYMF
MQKYPHTHLVQQANPRGSAGPCCTPTKMSPINMLYFNDKQQIIYGKIPGMV
VDRCGCS

Fig. 14J

SEQ ID NO:10 Human BMP-11 mature - DNA sequence

AACCTGGGTCTGGACTGCGACGAGCACTCAAGCGAGTCCCGCTGCTGCCG
ATATCCCCTCACAGTGGACTTTGAGGCTTTCGGCTGGGACTGGATCATCG
CACCTAAGCGCTACAAGGCCAACTACTGCTCCGGCCAGTGCGAGTACATG
TTCATGCAAAAATATCCGCATACCCATTTGGTGCAGCAGGCCAATCCAAG
AGGCTCTGCTGGGCCCTGTTGTACCCCCACCAAGATGTCCCCAATCAACA
TGCTCTACTTCAATGACAAGCAGCAGATTATCTACGGCAAGATCCCTGGC
ATGGTGGTGGATCGCTGTGGCTGCTCT

Fig. 14K

SEQ ID NO:11 Human BMP-11 propeptide - protein
sequence

AEGPAAAAAAAAAAAAAGVGGERSSRPAPSVAPDPGCPVCVWRQHSRELR
LESIKSQILSKLRLKEAPNISREVVKQLLPKAPPLQQILDLHDFQGDALQP
EDFLEEDEYHATTETVISMAQETDPAVQTDGSPLCCHFHFSPKVMFTKVLK
AQLWVYLRPVPRPATVYLQILRLKPLTGEGTAGGGGGGRRHIRIRSLKIEL
HSRSGHWQSIDFKQVLHSWFRQPQSNWGIEINAFDPSGTDLAVTSLGPGAE
GLHPFMELRVLENTKRSRR

SEQ ID NO:12 Human BMP-11 propeptide - DNA
sequence

[illegible]

Fig. 14M

SEQ ID NO:13 GDF-8 signal sequence - protein
sequence

MQKLQLCVYIYLFMLIVAGPVDL

Fig. 14N

SEQ ID NO:14 BMP-11 signal sequence - protein
sequence

MVLAAPLLLGFLLLALELRPRGEA

Fig. 14Q

SEQ ID NO:15 Human IgG1-Fc - protein sequence

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDV
SHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK
EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCL
VKGFYPSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQ
GNVFSCSVMHEALHNHYTQKSLSLSPGK

Fig. 14P

SEQ ID NO:16 Human IgG1-Fc modified - protein
sequence

DKTHTCPPCPAPEALGAPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDP
EVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCK
VSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY
PSDIAVEWESNGQPENNYKTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS
CSVMHEALHNHYTQKSLSLSPGK